FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 16:59:02 ON 10 DEC 2004

L1	30678	S HUMAN TISSUE FACTOR OR (TF)
L2	2181226	S ANTIBOD?
L3	2784	S L1 (P) L2
L4	2033	S L1 (S) L2
L5	10997	S HUMANIZED
L6	105086	S CHIMERIC
L7	33	S L4 (P) L5
L8	25	DUP REM L7 (8 DUPLICATES REMOVED)
L9	5	S L8 AND PY<=2000
L10	27	S L4 (P) L6
L11	18	DUP REM L10 (9 DUPLICATES REMOVED)
L12	5	S L11 AND PY<=2000
L13	8	DUP REM L9 L12 (2 DUPLICATES REMOVED)
L14	5410	S BISPECIFIC
L15	7	S L4 (P) L14
L16	4	DUP REM L15 (3 DUPLICATES REMOVED)
L17	531424	S THROMBOSIS OR COAGULAT?
L18	662	S L4 (P) L17

IN Wong, Hing C.; Jiao, Jin-An
SO U.S. Pat. Appl. Publ., 28 pp., Cont.-in-part of U.S. Ser. No. 293,417.
CODEN: USXXCO
TI Anti-human tissue factor antibodies for inhibiting blood coagulation and preventing and treating septic shock, inflammation and thrombosis
AB Disclosed is a method for treating blood coagulation in a mammal that has or is suspected of having septic shock syndrome. In one embodiment, the method includes administering to the mammal an effective amt. of an antibody that binds tissue factor in a way that excludes Factor X (FX) binding. The invention has a wide range of useful applications including use to inhibit unwanted blood coagulation assocd. with sepsis, or blood clot or thrombosis assocd. with invasive medical procedure such as surgery or transplant or medical implementation (catheter, stent or other medical device). The antibodies may also be combined with anticoagulant, anti-platelet and/or thrombolytic agent to boost or prolong inhibition of blood coagulation.

L13 ANSWER 2 OF 8 MEDLINE on STN
AU Rippmann J F; Pfizenmaier K; Mattes R; Rettig W J; Moosmayer D
SO Biochemical journal, (2000 Aug 1) 349 Pt 3 805-12.
Journal code: 2984726R. ISSN: 0264-6021.
TI Fusion of the tissue factor extracellular domain to a tumour stroma specific single-chain fragment variable antibody results in an antigen-specific coagulation-promoting molecule.
AB Solid tumours growing beyond a size of 1-2 mm in diameter induce supporting connective tissue structures, the tumour stroma, comprising activated fibroblasts and newly formed blood vessels, embedded in an extracellular matrix. The selective destruction of this tissue or the inhibition of its function (e.g. tumour neoangiogenesis) may result in the destruction of tumour nodules, thus providing novel opportunities for tumour therapy. Our approach aims at an antibody-mediated induction of coagulation in tumour nodules to cut off their blood supply. As a target structure the fibroblast activation protein (FAP) is used, which is specifically and abundantly expressed on the activated fibroblasts of the tumour stroma. We constructed a fusion protein comprising a single-chain module of a FAP-specific humanized antibody [single-chain fragment variable (scFv) OS4] and the extracellular domain of human tissue factor. The fusion protein, designated TFOS4, was produced in the Proteus mirabilis protoplast expression system with a yield of 15 microg/ml. Biochemical characterization of TFOS4 revealed high-affinity binding to cellular FAP. Further, TFOS4 bound to factor VIIa and also exerted allosteric activation of factor VIIa. A complex of TFOS4 and factor VIIa bound to FAP-expressing cells efficiently generated activated factor X. Finally, cell-bound TFOS4 selectively induced plasma coagulation, implying its activity under physiological conditions, notably with relevant concentrations of coagulation factors and their natural inhibitors. These findings suggest that TFOS4 has the potential to increase the procoagulant state in a cell-type-specific fashion. No systemic coagulation or side effects were observed when TFOS4 was injected intravenously into normal mice, indicating the biosafety and specificity of the recombinant protein.

L13 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
IN Sato, Koh; Adachi, Hideki; Yabuta, Naohiro
SO PCT Int. Appl., 292 pp.
CODEN: PIXXD2
TI Humanized antibody against human tissue factor (TF) and process for constructing humanized antibody
AB A humanized antibody against tissue factor (TF) which comprises: A. a humanized H chain contg. (1) an H chain V region contg. the H chain CDR of a mouse monoclonal antibody against TF and the H chain FR of a human antibody, and (2) the H chain C region of a human antibody; and B. a humanized L chain contg. (1) an L chain V region contg. the L chain CDR of a mouse monoclonal antibody against TF and the L chain FR of a human antibody, and (2) the L chain C region of a human antibody. The mouse monoclonal antibody CDR is grafted into the human antibody to construct the humanized V region. Next, the FR thereof is replaced by the corresponding FR of another human antibody with a high homol., thus detecting a highly active humanized antibody. The prepd. chimeric antibodies are useful for treating disseminated intravascular coagulation syndrome.

IN Joliffe, Linda K.; Zivin, Robert A.; Pulito, Virginia L.
SO PCT Int. Appl., 140 pp.
CODEN: PIXXD2
TI CDR-grafted anti-tissue factor antibodies and methods of use thereof
AB The present invention provides CDR-grafted antibodies against human tissue factor that retain the high binding affinity of rodent monoclonal antibodies against tissue factor but have reduced immunogenicity. The present humanized antibodies are potent anticoagulants and are thus useful in the treatment and prophylaxis of human thrombotic disease. The invention also provides methods of making the CDR-grafted antibodies and pharmaceutical compns. for the attenuation or prevention of coagulation.

IN Thorpe, Philip E.; Edgington, Thomas S.
SO PCT Int. Appl., 325 pp.
CODEN: PIXXD2
TI Methods and bifunctional ligands for specific tumor inhibition by blood coagulation in tumor vasculature
AB Bispecific binding ligands are provided which bind through a 1st binding region to a disease-related target cell, e.g. a tumor cell or tumor vasculature; the 2nd region has coagulation-promoting activity or is a binding region for a coagulation factor. Since tumor vasculature is prothrombotic and is predisposed towards coagulation, these targeted coagulants selectively induce blood coagulation in vessels supplying the tumor and cause death of tumor cells. The bispecific binding ligand may be a bispecific (monoclonal) antibody, or the 2 ligands may be connected by a (selectively cleavable) covalent bond, a chem. linking agent, an avidin-biotin linkage, etc. The target of the 1st binding region may be a cytokine-inducible component, and cytokine may be release in response to a leukocyte-activating antibody; this may be a bispecific antibody which crosslinks activated leukocytes with tumor cells. Alternatively, the target of the 1st binding region may be a component (e.g. E- or P-selectin) which is inducible by thrombin, where thrombin prodn. is induced by administration of a bispecific antibody which binds to a tumor cell and to tissue factor, prothrombin, factor VII/VIIa, factor IX/IXa, etc. Thus, a coaguligand (bispecific antibody capable of targeting a coagulant to a tumor site) was prepd. by chem. coupling an Fab' fragment from monoclonal antibody B21-2 (which reacts with I-Ad antigen expressed on A20 B-cell lymphoma cells and on the vasculature of C1300 transfectant mouse tumors) with an Fab' fragment from monoclonal antibody 10H10 (which reacts with human tissue factor). Incubation of A20 cells with this bispecific antibody and recombinant human truncated tissue factor resulted in tethering of tissue factor to the cells; plasma added to the A20 cell-tissue factor complex coagulated rapidly. Kits comprising the bifunctional ligand, a 2nd ligand, and optionally a drug for conjunctive therapy are described.

AU Huang X; Molema G; King S; Watkins L; Edgington T S; Thorpe P E

SO Science, (1997 Jan 24) 275 (5299) 547-50.
Journal code: 0404511. ISSN: 0036-8075.

TI Tumor infarction in mice by antibody-directed targeting of tissue factor to tumor vasculature.

AB Selective occlusion of tumor vasculature was tested as a therapy for solid tumors in a mouse model. The formation of blood clots (thrombosis) within the tumor vessels was initiated by targeting the cell surface domain of human tissue factor, by means of a bispecific antibody, to an experimentally induced marker on tumor vascular endothelial cells. This truncated form of tissue factor (tTF) had limited ability to initiate thrombosis when free in the circulation, but became an effective and selective thrombogen when targeted to tumor endothelial cells. Intravenous administration of the antibody-tTF complex to mice with large neuroblastomas resulted in complete tumor regressions in 38 percent of the mice.

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	0	10/089,501	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/10 11:29
S2	1619	hiroyuki near saito.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/10 11:30
S3	2	takehisa near kitazawa.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/10 11:31
S4	1	kazutaka near yoshihashi.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/10 11:31
S5	0	kunihiro near hatori.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/10 11:32
S6	45	kunihiro near hattori.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/10 11:32
S7	543	(human adj tissue adj factor)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/10 11:34
S8	1	S2 AND S7	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/10 11:33
S9	2	S6 AND S7	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/10 11:33
S11	200605	antibod$3	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/10 11:34
S12	372	S7 and S11	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/10 11:34
S13	21152	(human adj tissue adj factor) OR (TF)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/10 11:34
S14	2656	S13 same S11	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/10 11:35

S15	20014	humanized	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/10 11:35
S16	45404	chimeric	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/10 11:36
S17	48	S14 same S15	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/10 11:54
S18	61	S14 same S16	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/12/10 11:54
S19	1	("5346991").PN.	USPAT	OR	OFF	2004/12/10 14:17

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